

Comparing Differences in Alzheimer's Disease Classification between Structural and Resting-State Functional MRI Biomarkers

Gang Chen¹, Chunming Xie¹, Guangyu Chen¹, Wenjun Li¹, B. Douglas Ward¹, Jennifer L Jones², Malgorzata Franczak², Piero G Antuono², and Shi-Jiang Li¹
¹Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, ²Department of Neurology, Medical College of Wisconsin, Milwaukee, WI, United States

Introduction: Resting-state functional magnetic resonance imaging (RfMRI) and structural MRI have been employed in Alzheimer's Disease (AD) classification (1–4). However, researchers are not always certain as to how to improve classification when data from both of these modalities are available. In this study, the classification results of the two techniques were compared, using the same study cohort.

Methods: Sixty-five AD and 136 cognitively normal (CN) subjects' RfMRI data were included in the study. Data used in this work were from the Medical College of Wisconsin (MCW) fMRI Data Bank and the AD Neuroimaging Initiative (ADNI) database (adni.loni.ucla.edu).

RfMRI-based classification: The subjects were randomly assigned to a training and evaluation cohort. The training cohort defined the RfMRI biomarker and the evaluation cohort evaluated the classification power of the biomarker (i.e., functional connectivity, FC). To train the classifier, the FC of 90 brain regions (5) was employed. The regions were sorted by their classification accuracies in the training data set. Using the region that ranks the first will ideally provide best separation, however, it suffers from reduced classification power caused by intersubject variation. Using more regions may reduce the effect of intersubject variation, however, it will ideally provide less separation. So, a trade-off has to be achieved. We used the *leave-one-out* (LOO) method to determine the optimal number of regions and evaluate the classification accuracy in the evaluation data set. Specifically, the evaluation data set was divided into two parts: the LOO subject and the N-1 subjects. The latter determined the optimal number of regions (x) that provides best classification accuracy for the N-1 subjects. Then the x regions classified the LOO subjects. The procedure was repeated, and every subject in the evaluation data set was left out once. The classification results of the N LOO subjects were then compared with the known disease status to calculate the classification accuracy. The classification accuracy can be affected by how the subjects were assigned to the training and evaluation cohort. To obtain the mean and standard deviation of the classification accuracy, the above steps were repeated 100 times.

Structural MRI-based classification: The same procedure discussed above was used, except the structural MRI information (gray matter concentration (GMC) in the 90 brain regions) was used instead of the RfMRI information.

Congruous and incongruous results between structural and resting-state functional MRI biomarkers: The classification results using the RfMRI information and the structural MRI information did not always agree. In each LOO step, if the results didn't agree, the LOO subject was then classified as having an incongruous status. The classification accuracy was then evaluated on the subjects who were congruously classified.

Results: Figs. 1 and 2 show the regions that were employed as the classifiers. The color bar shows the frequency that the regions were chosen in the classification. RfMRI-based classification provided an accuracy of 73.5±5.8%. Structural MRI-based classification provided an accuracy of 84.0±5.3%. The classification using RfMRI and structural MRI provided congruous classification on 71.0±5.8% of the subjects with an accuracy of 90.4±4.3%. There were no congruous classification made on 29.0±5.8% of the subjects. The results are summarized in Fig. 3.

Among the incongruously classified subjects, 48.48±8.83% had an AD status (80.7±12.9% of these subjects had AD type GMC but CN type FC; the rest of the 19.3±12.9% subjects had CN type GMC but AD type FC).

Among the incongruously classified subjects, 51.52±8.83% had a CN status (43.7±18.3% of these subjects had AD type GMC but CN type FC; 56.3±18.3% subjects had CN type GMC but AD type FC).

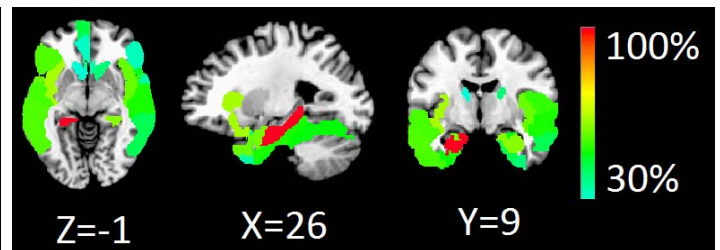
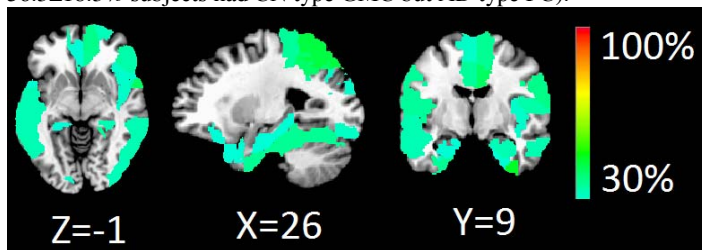


Fig 1. Regions maximizing the RfMRI based classification

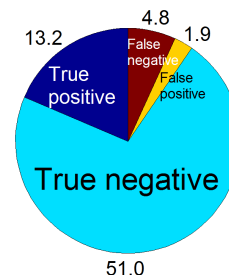
Fig 2. Regions maximizing the structural MRI based classification

Discussion: We compared AD classification technique differences using structural and resting-state functional MRI biomarkers. When the RfMRI classification result agrees with the structural MRI classification result, the subjects can be classified with 90% accuracy. The large portion of CN subjects in the data explains the high true negative rate. The incongruous GMC and FC characteristics may explain the lower classification accuracy using either technique alone. It is hypothesized that the incongruously classified CN subjects may have a higher chance to convert to AD because of their abnormal GMC or FC. The incongruously classified AD subjects may respond better to specific treatments because of their intact GMC or FC. These hypotheses will be tested in our future studies.

References: 1. Li SJ, et al., 2002 Radiology, 225:253-9; 2. Chen G, et al., 2011 Radiology, 259:213-21; 3. Fan Y, et al., 2008 NeuroImage 41:277–85; 4. Westman E, et al., 2011 NeuroImage 58:818–28; 5. Tzourio-Mazoyer et al., NeuroImage 2002 15: 273-89;

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Congruously classified subjects



Incongruously classified

AD subjects

CN subjects

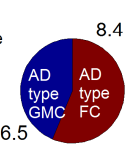
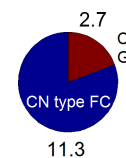


Fig3. Congruous and incongruous results between structural and resting-state functional MRI biomarkers